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The goal of this training program is to significantly extend our existing, highly successful Doctoral Training Program in Tumor Biology and several Cancer Center mechanisms that provide traditional postdoctoral training and junior faculty career development. The program integrates faculty from the Lombardi Comprehensive Cancer Center programs in Cancer Prevention and Control and Cancer Genetics, makes use of the existing organizational structure of the Interdisciplinary Doctoral Training Program in Tumor Biology, and incorporates a multi-disciplinary faculty who are devoted to research and education in breast cancer.

To date, 8 fellows have been recruited into the program (4 classes) and 4 new courses of study were added to our program. Fellows have published 8 papers and 3 abstracts, and 2 fellows went on to academic faculty jobs; other fellows in the program continue to make good career development progress.

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## COMPREHENSIVE POSTDOCTORAL TRAINING PROGRAM IN BREAST CANCER BIOLOGY

### INTRODUCTION

The Comprehensive Postdoctoral Training Program in Breast Cancer Biology has successfully completed its fourth year. The goal of the program is to significantly extend our existing, highly successful Doctoral Training Program in Tumor Biology and several Cancer Center mechanisms that provide traditional postdoctoral training and junior faculty career development. The education and training of new investigators is essential to our progress in the prevention, detection, diagnosis, and treatment of breast cancer. The Postdoctoral Training Program in Breast Cancer provides comprehensive career development and integrates interactive research in the basic biology of breast cancer, formal and informal course work in key areas, and individualized guidance in career development. The program is enriched with both new and existing courses of interest to postdoctoral fellows covering scientific writing, teaching methodologies, scientific resources and technologies for cancer research, ethics in science, career development seminar series, and provides a firm foundation in the skills needed to succeed in a career science, as well as a focused research experience in basic breast cancer biology in a strong laboratory environment. Additional programmatic activities include monthly Oncology Grand Rounds, weekly Tumor Biology Seminar Series, and weekly journal clubs. The program makes use of the existing organizational structure of the Interdisciplinary Doctoral Training Program in Tumor Biology and incorporates a multi-disciplinary faculty who are devoted to research and education in breast cancer.

Postdoctoral fellows are given the opportunity to seek research and career advice from a number of senior faculty. The further development of this structured Tumor Biology Postdoctoral training program will provide excellent preparation for successful careers in cancer research.

### BODY

#### *Training and Research Accomplishments*

The accomplishments of this program include the recruitment and progress of postdoctoral fellows. In the past 10 years, over 100 postdoctoral fellows have been trained by our Tumor Biology program preceptors. These fellows have an outstanding record of research productivity and peer-reviewed publication, and over 50% of them have obtained academic faculty level positions.

In the first year of the program, two postdoctoral fellows, Fadwa Attiga, Ph.D. and Tushar Deb, Ph.D., were recruited to the program. Dr. Attiga successfully

completed her postdoctoral fellowship in Dr. Stephen Byer's lab, researching the cross regulation between the IKK and the beta-catenin signaling pathways in breast and colon cancers. Her research topics included a study of how different kinases regulate the level of oncogene beta-catenin in tumor cells and identification of the key players in the signaling cascades that alter the beta-catenin protein level and transcriptional activity in tumors. A paper is now under submission to Mol. Cell. Biol. describing Dr. Attiga's work, and she subsequently took a faculty position as Instructor of Biology at American University.

Dr. Deb, has completed his postdoctoral fellowship in Dr. Robert Dickson's lab and is now a Research Instructor of Oncology at Georgetown University. The Department of Oncology is supporting his promotion to Research Assistant Professor later this year. The main focus of Dr. Deb's research is to explore the EGF cell-survival signaling in transgenic MMTV-c-Myc expressing mammary epithelial cells. Proto-oncogene c-Myc sensitizes these cells to apoptosis in absence of serum. A novel role of a calmodulin dependent kinase in this survival signaling process is also being explored. Dr. Deb just published two papers in J. Biol. Chem. describing this work.

Marcia Noble, Ph.D., and Kerrie O'Brien, Ph.D., were recruited into the second year of the program. Dr. Noble began her postdoctoral fellowship in September 2001, under collaborative mentorship of Dr. Michael Johnson and Dr. Robert Dickson. Dr. Noble's research focus was on the mechanism of VEGF to promote breast cancer metastases in transgenic mouse models. Dr. Noble completed her postdoctoral fellowship and is now an FASS Congressional Science Policy Fellow. Dr. Noble recently submitted a paper on her research to Cancer Research. A second paper was just published in In Vitro Cell Biology (Animal). Dr. O'Brien began her postdoctoral fellowship in March 2002 under mentorship of Dr. Robert Clarke. Dr. O'Brien's research focuses on the resistance to retinoids in breast cancer. She recently published papers in Oncogene and Cancer Research.

Constanze Hample, PhD was recruited into the third class of the postdoctoral fellowship program in September 2002 in the laboratory of Dr. Stephen Byers. Dr. Hample is currently focusing on Cadherin-11 and breast cancer invasion, and is preparing a paper for submission.

Dr. Ming-Shuye Lee, Dr. Fransiscus Utama, and Ayesha Shajahan were recruited to the fourth class of this program. Dr. Lee began in September, 2003 in Dr. Dickson's laboratory, Dr. Utama began in January, 2004 with Dr. Rui, and Dr. Shajahan is scheduled to begin in August 2004 with Dr. Clarke.

As noted earlier, our Postdoctoral Program incorporates elements of our existing Tumor Biology Ph.D. program, as well as new, Postdoctoral Training-specific elements as a part of a Breast Cancer Prevention Track. In addition to the existing core courses of the Interdisciplinary Doctoral Training Program in Tumor Biology, new course components have been incorporated into the Breast Cancer Prevention track in Spring 2002. These include a course in Biostatistics, *Applied Biostatistics*, that has been

refocused on statistical design and methodology for research rather than biostatistics theory, and a Cancer Genetics course, *Genetics, Health, and Society in the 21<sup>st</sup> Century*, which focuses on practical and ethical questions raised by genetic information and technology. Both courses had very successful first and second years and will continue to be offered. A new course in Genetics, *Human and Microbial Genetics*, and an additional new course, *Cancer Prevention and Epidemiology* will be offered next Spring.

### KEY ACCOMPLISHMENTS

- *Recruitment of Trainees and Progress of Trainees:*
  - Three postdoctoral fellows have been recruited into the fourth class (beginning September, 2003) of the Comprehensive Postdoctoral Training Program in Breast Cancer Biology: Dr. Lee (with Dr. Robert Dickson), Dr. Utama (with Dr. Halgeir Rui), and Dr. Shajahan (with Dr. Robert Clarke).
  - One postdoctoral fellow, Dr. Constanze Hampel, was recruited into the third class of the program. Dr. Hampel began her fellowship in September, 2002 in the laboratory of Dr. Stephen Byers.
  - Two postdoctoral fellows were recruited into the second class of the Comprehensive Postdoctoral Training Program In Breast Cancer Biology (beginning September, 2001): Marcia Noble, Ph.D., and Kerrie O'Brien, Ph.D. Dr. Noble began the program in Dr. Michael Johnson's and Dr. Robert Dickson's laboratories, and has taken a Federal Government position in Science Policy. Dr. O'Brien is working in Dr. Robert Clarke's laboratory.
  - Dr. Deb, from the first class (beginning September, 2000), has successfully completed his postdoctoral fellowship and is currently a Junior Faculty member in the Department of Biology at Georgetown University.
  - Dr. Attiga, from the first class (beginning September, 2000), completed her first year with Dr. Stephen Byers and accepted a junior faculty position at American University.
- *New Courses:*
  - *Human and Microbial Genetics (Elective Course)*
  - *Applied Biostatistics (Core Course)*
  - *Genetics, Health and Society in the 21<sup>st</sup> Century (Elective Course)*
  - *Cancer Prevention and Epidemiology (Core Course)*

### REPORTABLE OUTCOMES

- *Career Placement*
  - Dr. Attiga accepted a position as Instructor of Biology at American University (2002)

- Dr. Deb accepted a position as Instructor of Oncology at Georgetown University (2003)
- Dr. Noble accepted a position as an FASS Congressional Science Policy Fellow (2004)
- *Publications:*
  - Clarke R, Liu MC, Bouker KB, Gu Z, Lee RY, Zhu Y, Skaar TC, Gomez B, **O'Brien K**, Wang Y, and Hilakivi-Clarke LA. Antiestrogen resistance in breast cancer and the role of estrogen receptor signaling. Oncogene 22:7316-7339, 2003.
  - Bouker KB, Skaar TC, Fernandez DR, **O'Brien KA**, Riggins RB, Cao D, Clarke R. Interferon Regulatory Factor-1 mediates the proapoptotic but not cell cycle arrest effects of the steroidal antiestrogen ICI 192,780 (Faslodex, Fulvestrant), Cancer Res., 64:4030-4039, 2004.
  - Pei XF, **Noble M**, Johnson MD, Rosfjord E, and Dickson RB. Expant-Cell Culture of Primary Mammary Tumors from MMTV-c-Myc Transgenic Mice. In Vitro Cell Biology ( Animal) 40:14-21 2004 .
  - Teo M, **Attiga F**, Jarrett C, Zipper L, Waldman T, Gaynor R, Pestell R and Byers S. The IKK complex mediates TNF aregulation of  $\beta$ -catenin signaling. Molecular and Cellular Biology, submitted.
  - **Noble M**, Rosfjord E, Deming S, Chepko G, Carbott D, LaRoche WJ, Anver M, Sharp R, Celli G, Russell RG, Johnson MD, Merlino GT, and Dickson RB: MMTV-LTR-c-myc/VEGF mice: a metastatic model, Cancer Res., submitted.
  - **Deb TB**, Coticchia CM, and Dickson RB, Calmodulin-mediated activation of Akt regulates survival of c-Myc over-expressing mouse mammary carcinoma cells. J. Biol. Chem., in press, 2004.
  - Fan Y-X, Wong L, **Deb TB**, Johnson GR , Ligand regulates EGF receptor kinase specificity, J. Biol. Chem., in press, 2004.
  - **Hampel C**, Blaschuk O, Rowlands T, and Byers S. Small molecule antagonists of cadherin-11 function alter breast cancer cell invasion and VEGF expression, in preparation.
- *Abstracts:*
  - **Deb, T**, and Dickson, R. Calmodulin as a Positive Modulator of EGF Survival Signaling in MMTV-C-MYC Mouse Mammary Epithelial Cells. DOD ERA of Hope Meeting, Orlando, FL, 2002.

- **Noble M**, Rosfjord EC, Sharp R, Merlino G, and Dickson RB. Ectopic VEGF Expression Promotes Metastasis in Bitransgenic Breast Cancer Model. DOD ERA of Hope Meeting, Orlando, FL, 2002.
- **Teo M**, **Attiga F**, Jarret C, and Byers S. Cytokine Regulation of  $\beta$ -catenin Signaling. Fourth Annual Lombardi Research Fair. Georgetown University Medical Center, Washington, D.C. 2002.

### CONCLUSIONS

The goal of the program is to significantly extend our existing, highly successful Postdoctoral Training Program in Cancer with a new specialization in Breast Cancer Biology. We have successfully recruited 4 classes of Comprehensive Postdoctoral Training Program in Breast Cancer Biology (8 fellows) and have created 4 new courses. In addition, we have placed 3 fellows in their next career positions in academics and in science policy positions, while 5 fellows are still in training here.